

Structure and mechanism of the tripartite CusCBA heavy-metal efflux complex.

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Public Summary:

Gram-negative bacteria frequently expel toxic chemicals through tripartite efflux pumps that span both the inner and outer membranes. The three parts are the inner membrane, substrate-binding transporter (or pump); a periplasmic membrane fusion protein (MFP, or adaptor); and an outer membrane-anchored channel. The fusion protein connects the transporter to the channel within the periplasmic space. One such efflux system CusCBA is responsible for extruding biocidal Cu(I) and Ag(I) ions. We previously described the crystal structures of both the inner membrane transporter CusA and the MFP CusB of *Escherichia coli*. We also determined the co-crystal structure of the CusBA adaptor-transporter efflux complex, showing that the transporter CusA, which is present as a trimer, interacts with six CusB protomers and that the periplasmic domain of CusA is involved in these interactions. Here, we summarize the structural information of these efflux proteins, and present the accumulated evidence that this efflux system uses methionine residues to bind and export Cu(I) and Ag(I). Genetic and structural analyses suggest that the CusA pump is capable of picking up the metal ions from both the periplasm and the cytoplasm. We propose a stepwise shuttle mechanism for this pump to export metal ions from the cell.

Scientific Abstract:

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